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Job Strain and Risk Indicators for Cardiovascular Disease in Young Female Nurses

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This study examined the possible effects of job demands, decision latitude, and job-related social support on risk indicators for cardiovascular disease (CVD) in 165 female nurses. Job strain was measured with the Job Content Questionnaire; CVD risk was measured with insulin, total cholesterol, triglyceride (TG), high-density lipoprotein cholesterol (HDL-C), fibrinogen, tissue-type plasminogen activator (tPA) antigen, tPA activity, plasminogen activator inhibitor-1 antigen, and blood pressure. Multivariate analysis of covariance and regression analyses revealed no effects of either job strain or social support on these risk indicators. All risk indicators deteriorated with age and body mass index. Oral contraceptive use improved fibrinolytic potential and increased HDL-C but had adverse effects on TG levels. Results suggest that in healthy young women job strain is not associated with an unfavorable metabolic or fibrinolytic risk profile.

Key words: job demands, decision latitude, social support, insulin resistance syndrome, fasting insulin, lipids, fibrinogen, tissue-type plasminogen activator, plasminogen activator inhibitor, blood pressure

Previous studies have reported an association between organizational and psychosocial features of the work environment and cardiovascular disease (CVD). Most of these studies used the Demand Control model to summarize the detrimental effects of the work setting in the concept of *job strain*, a combination of high job demands and low job decision latitude (Karasek & Theorell, 1990; Kristensen, 1989, 1995; Schnall, Landsbergis, & Baker, 1994; Theorell & Karasek, 1996). An extension of the Demand Control model posits that lack of social support at work further increases risk for CVD (Johnson & Hall, 1988; Johnson, Stewart, Hall, Fredlund, & Theorell, 1996; Uchino, Cacioppo, & Kiecolt-Glaser, 1996). Prospective evidence suggests a causal effect of job strain on cardiovascular morbidity and mortality (Hammar, Alfredsson, & Johnson, 1998; Johnson et al., 1996; Johnson & Hall, 1988), but the underlying mechanisms are poorly understood.

Job strain may influence the traditional cardiovascular risk factors, such as smoking, increased blood pressure (BP) and

plasma cholesterol levels, lack of exercise, and unfavorable dietary habits (Karasek & Theorell, 1990; Kristensen, 1989; Schneiderman & Skyler, 1996; Theorell & Karasek, 1996). In their review of 21 articles on this topic, Schnall et al. (1994) concluded that job strain appears to mainly affect BP. A recent prospective study confirmed the effects of job strain on BP by showing a significantly higher rise in ambulatory BP across a period of 3 years in men with high job strain (Schnall, Schwartz, Landsbergis, Warren, & Pickering, 1998). However, studies of women more often fail to find a job-strain effect on BP than studies of men, which Schnall et al. (1994) attributed to the lower prevalence of hypertension at the employable age in women. Social support has been found to be associated with lower BP in the majority of studies (Uchino et al., 1996), but the effects seem to apply only to social support received from family and friends rather than job-related social support.

Studies on male or combined male and female populations failed to find associations between job strain and total cholesterol (TC; Greenlund et al., 1995; Gyntelberg et al., 1998; Kawakami, Haratani, & Araki, 1998; Netterstrøm, Kristensen, Damsgaard, Olsen, & Sjø, 1991; Weidner, Boughal, Connor, Pieper, & Mendell, 1997), high-density lipoprotein cholesterol (HDL-C; Gyntelberg et al., 1998; Netterstrøm et al., 1991; Weidner et al., 1997), or triglyceride (TG; Netterstrøm et al., 1991; Weidner et al., 1997). By use of the Siegrist Effort Reward Imbalance model (Siegrist, Peter, Junge, Cremer, & Seidel, 1990), high intrinsic effort, an indication of higher work stress, was found to be associated with increased low-density lipoprotein cholesterol (LDL-C) levels in both male and female populations (Peter et al. 1998; Siegrist, Peter, Cremer, & Seidel, 1997), although a recent study in men failed to replicate this effect (Vrijkotte, Van Doornen, & De Geus,

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1999). In their review, Niaura, Stoney, and Herbert (1992) suggested that job strain or other forms of chronic stress have little impact on lipids and lipoproteins. However, in a female population a detrimental effect on HDL-C levels was reported, although only for one of the components of job strain, low decision latitude (Wamala, Wolk, Schenk-Gustafsson, & Orth-Gomér, 1997). In summary, there is some evidence for job-strain or job-related social-support effects on BP and lipids in women, but it is currently not strong. Even if BP and lipid levels respond to job strain, these risk factors can only partially explain the effects of job strain on CVD. For instance, in the Kuopio Ischemic Heart Disease Risk Factor Study, the 4-year progression of carotid atherosclerosis in men was predicted by job strain, after correction for BP and cholesterol levels (Lynch, Krause, Kaplan, Salonen, & Salonen, 1997).

Hypertension, hypercholesterolemia, and hypertriglyceridemia are only three aspects of a broader cluster of risk indicators that has been named the Insulin Resistance Syndrome (IRS; Reaven, 1988, 1996). Further aspects of this syndrome are hyperinsulinemia, central obesity, and impaired fibrinolysis (Asplund-Carlson, Hamsten, Wiman, & Carlson, 1993; Eliasson, Ervin, & Lundblad, 1994; Meigs et al., 2000; Reaven, 1988, 1996; Vague, Raccach, & Scelles, 1995). There is still no consensus about the cause of the IRS, but chronic stress appears to negatively influence all aspects of the syndrome (Schneiderman & Skyler, 1996). Stress-induced increases in sympathetic activation with increased levels of catecholamines are found to lead to obesity (Björntorp, 1997; Wamala, Wolk, & Orth-Gomér, 1997) and dysregulation of BP (Julius & Jamerson, 1994), insulin metabolism (Brindley & Rolland, 1989; Schneiderman & Skyler, 1996), and lipid metabolism (Niaura et al., 1992). These effects are amplified by activation of the hypothalamic-pituitary-adrenal (HPA) axis and subsequent release of cortisol, which further enhances the pathogenesis of insulin resistance (Holmång & Björntorp, 1991). Women reporting high levels of chronic stress, measured as neuroticism and trait anxiety, had in general higher levels of cortisol and insulin resistance (Tuiten et al., 1995). In a group of middle-aged men, psychosocial stress correlated with hyperinsulinemia (Räikkönen, Keltikangas-Järvinen, Adlercreutz, & Hautanen, 1996; Räikkönen, Keltikangas-Järvinen, & Hautanen, 1994), although this effect was not replicated by Vrijkotte et al. (1999).

Apart from hypertension and the atherosclerotic risk, job-strain-induced reactivity of the autonomic nervous system may also change the balance in coagulation and fibrinolysis (thrombotic risk). Plasma fibrinogen would be a first possible target for job-strain effects because it is an established risk factor for CVD (Ernst & Resch, 1993; Kannel, D'Agostino, & Belanger, 1992; Meade et al., 1996). Four studies in men have indeed reported higher fibrinogen in high-work-stress (Siegrist et al., 1997) or high-job-strain groups (Markowe et al., 1985; Netterstrøm et al., 1991) or during periods of high stress (Frimerman, Miller, Laniado, & Keren, 1997), although three others failed to find an association (Folsom et al., 1993; Mattiasson & Lindgarde, 1993; Møller & Kristensen, 1991). The source of discrepancy in results for men is unclear other than that the positive studies were more often conducted in white-collar workers. In women, several studies failed to find an association with overall job strain (Folsom et al., 1993; Gyntelberg et al., 1998; Tsutsumi, Theorell, Hallqvist, Reuterwall, & De Faire, 1999), job-related social support (Gyntelberg et al., 1998), or

general social support (Folsom et al., 1993). One study did find higher fibrinogen with high job strain and low social support ("negative boss relationship"; Davis, Matthews, Meilahn, & Kiss, 1995). However, at least three studies reported higher fibrinogen in women with low decision latitude (Brunner et al., 1996; Tsutsumi et al., 1999; Wamala et al., 1999), suggesting that fibrinogen may be sensitive only to the low-control aspect of job strain.

Only a few studies have appeared on the effects of job strain or job-related social support on two important thrombotic risk indicators: plasminogen activator inhibitor-1 (PAI-1) and tissue-type plasminogen activator activity (tPA-act). tPA plays a crucial role in fibrinolysis by destroying intravascular fibrin clots. PAI-1 regulates the concentration of tPA-act by continuously forming inactive tPA-PAI complexes in a well-characterized bimolecular reaction (Kluft, 1994; Sprengers & Kluft, 1987). The resulting disturbance between coagulation and fibrinolysis is thought to play an important role in the formation of arterial thrombus (Juhan-Vague, 1996; Markovitz & Matthews, 1991). tPA antigen (tPA-ag) has been positively associated with risk for myocardial infarction (Lowe et al., 1998; Ridker, Vaughan, Stampfer, Manson, & Hennekens, 1993). Although less consistently, increased PAI-1 and decreased tPA-act were associated with an increased risk for myocardial infarction (Hamsten et al., 1987; Lowe et al., 1998; Meade et al., 1996; Van Der Bom et al., 1997) as well as thrombosis (Juhan-Vague & Alessi, 1993; Wiman & Hamsten, 1991). In male blue-collar workers, Ishizaki et al. (1996) found tPA-act to be decreased in a group reporting high job demands. In male white-collar workers, Vrijkotte et al. (1999) found lower tPA-act and higher PAI-1 antigen (PAI-1-ag) in participants with excess overcommitment to work. The only study of women found a trend for lower PAI-1 activity with lower decision latitude (Wamala et al., 1999).

Most of the epidemiological research on the relation of job strain and CVD risk indicators introduced above was performed on men. CVD is, however, the leading health risk in women also, and employed women do indeed suffer from CVD (see, e.g., the Nurses' Health Study [Colditz, Manson, & Hankinson, 1997]). When comparing job characteristics between men and women, it seems that women are employed in occupations characterized by lower decision latitude and slightly higher job demands (Karasek & Theorell, 1990). In addition, the risk for CVD mediated through job strain is found to be twice as high in women compared with men (Olsen & Kristensen, 1991). The present study, therefore, examined the effects of job strain and job-related social support on CVD risk indicators in a group of women.

A striking characteristic of previous job-strain studies is that they have assessed only a subset of risk indicators, for example, only metabolic or hemostatic parameters. However, because of their additive or even synergistic effects, small elevations of multiple metabolic and fibrinolytic risk factors may be more detrimental than large deviations in one or some of these factors. To improve on previous studies, the present study evaluated the association of job demands, decision latitude, and social support with the full multivariate IRS cluster of metabolic and fibrinolytic risk indicators for CVD. These were assessed in a homogeneous group of young and healthy women so that variance attributable to other risk indicators, such as age, gender, socioeconomic status (SES), and type of work, was reduced.

Method

Participants

A total of 1,068 nurses from three nonacademic hospitals in Amsterdam received a Dutch version of the Job Content Questionnaire (JCQ). The 662 responders (62%) were asked to participate in an extensive examination of cardiovascular risk indicators that would include repeated blood sampling. Of the initial 662 responders, 331 agreed to participate in blood sampling. Of these 331 volunteers, 158 nurses were excluded from the final sample because they were employed less than 24 hr per week ($n = 76$); were not educated or employed as registered nurses ($n = 32$); were not in the right shift ($n = 16$; see *Procedure* section for further explanation); could not be contacted ($n = 14$); were pregnant, lactating, or on maternity leave ($n = 7$); changed jobs ($n = 7$); or were on sick leave, suffered from chronic disease, or received medical treatment for hypertension, hyperlipidemia, or depression ($n = 6$). To prevent stressful life events from confounding job-strain effects, 8 more nurses were excluded because they had experienced the severe disease or death of a closely related significant other (parent, spouse, or child), divorce, or any other event of major impact in the 3 months prior. A final total of 165 (mean age \pm SD = 33.7 ± 8.1 years; range = 22–55 years) female nurses were included in the study. All participants were healthy and did not receive treatment for hypertension, hyperlipidemia, or diabetes mellitus. As shown in Table 1, these participants did not differ from the nonparticipants on their score on job demands, decision latitude, or social support. All participants gave written informed consent before entrance to the study. The study was approved by the Ethics Committee of the Vrije Universiteit of Amsterdam.

Procedure

Blood samples were collected on two different days of the workweek. Participants were requested to fast and refrain from using alcohol, coffee, or tea after 11:00 p.m. the preceding night and to refrain from intense physical activity the preceding day. Blood was drawn between 7:00 and 7:30 a.m. at the workplace, with the participants in a sitting position, after a 15-min rest. The nurses had to work three successive early shifts, and the first shift had to be preceded by 2 nonworking days. The first blood sample was drawn at the first day of the early shift, and the second sample was drawn at the third day of that same shift. On the first day, participants' body weight (to the nearest 100 g) and height (to the nearest cm) were measured while the participants were in light clothing. On the second day, blood pressure was measured after the participants rested quietly in a recliner chair for 10 min. Two measurements were taken with a 2-min

interval with a SpaceLabs 90207 blood pressure measure device (SpaceLabs Medical, Redmond, WA). After testing we served breakfast.

Biomedical Measures

Blood was withdrawn according to the standardized European Concerted Action on Thrombosis assay procedures (Kluft & Meijer, 1996; Walker, 1992). Blood was drawn by venipuncture of the antecubital vein and sampled in six different Vacutainers in the following order: serum with clot activator (5 ml), serum (3 ml), Stabilyte (5 ml), citrate (5 ml), EDTA (3 ml), and NaF (2 ml). We mixed all Vacutainers by moving the Vacutainers 5 times "head over head" immediately after withdrawal. Fasting insulin (pmol/L) was determined with an immunoradiometric assay kit (Medgenix Diagnostics, Fleurus, Belgium) from blood taken out of the serum Vacutainer. Blood had to clot for 60 min at room temperature. Serum was separated by centrifugation at $2,000 \times g$ for 20 min at 4°C . Aliquots of serum were stored at -20°C . Values were multiplied by 0.139 to convert fasting insulin into mU/L. For determination of TC, TG, and HDL-C, the serum of the clot-activator Vacutainer was used. Blood was allowed to clot for 30–120 min at room temperature. Serum was separated by centrifugation at $2,000 \times g$ for 20 min at 4°C . Lipid determinations were performed on the same day with the Vitros 250 Clinical Chemistry analyzer (Johnson & Johnson, Rochester, NY) with Vitros clinical chemistry slides for TC and TG. HDL-C was determined in serum after a precipitation step with HDL-C precipitant (Boehringer Mannheim, Mannheim, Germany). All lipid values are given in mmol/L. Stabilyte blood was drawn for the determination of tPA-act. Citrated blood was withdrawn for determination of fibrinogen, tPA-ag, and PAI-1-ag. Immediately after withdrawal, we put the Vacutainers in melting ice and centrifuged them within 60 min ($2,000 \times g$, 20 min at 4°C). Aliquots of plasma were snap frozen immediately with solid carbon dioxide and stored at -80°C . tPA-act was measured with the biofunctional immunosorbent assay Chromolize tPA (Biopool, Umeå, Sweden). Results are expressed in IU/ml. Fibrinogen was determined with the STA coagulation analyzer (STAG-O, Asnières, France) and the STA fibrinogen kit (Boehringer Mannheim). The results are expressed in g/L. tPA-ag was measured with the enzyme immunoassay Imulyse tPA (Biopool). PAI-1-ag was measured with the enzyme immunoassay Innostat PAI-1 (Innogenetics, Zwijndrecht, Belgium). Results for tPA-ag and PAI-ag are expressed in ng/ml. The intraassay and interassay coefficients of variation were less than, respectively, 5.0% and 7.0% for fasting insulin, 4.0% and 6.0% for TC, 3.5% and 5.0% for HDL-C, 3.0% and 5.0% for TG, 5.0% and 7.0% for fibrinogen, 10.0% and 12.0% for tPA-ag, 7.5% and 10.0% for tPA-act, and 10.0% each for PAI-1-ag. For each of the blood variables, the samples were analyzed in the same batch. Moreover, the blood samples drawn from the same participant on repeated blood-withdrawal occasions were analyzed simultaneously on the same plate. No sample had been stored for more than 7 months.

From 34 nurses blood was drawn only at the first withdrawal day, and 4 nurses from whom blood was drawn twice failed to comply with our request not to eat breakfast. For these nurses, results for the missing day were estimated by using the results from the other measurement day. Imputation was based on regression of the first- and second-day measurements in the population with complete data.

Psychosocial and Behavioral Measures

In the present study, a self-administered Dutch version of the Job Content Questionnaire (Karasek, Pieper, & Schwartz, 1985), originating from the Dutch Monitor of Stress and Physical Load, was used (Houtman, Goudswaard, et al., 1998). The subscale Job Demands was assessed with five dichotomous items. Examples of the Job Demands items are "Do you have to do an excessive amount of work?" and "Is your job hectic?" Skill Discretion (five dichotomous items) and Decision Authority (seven dichotomous items) were combined into the subscale Decision Latitude. Exam-

Table 1
Job Strain Characteristics ($M \pm SD$) of the Original Population, the Population Willing to Partake in Blood Sampling, and the Final Population Eligible in View of the Inclusion and Exclusion Criteria

Job strain characteristic	Population		
	Original ($n = 662$)	Blood sampling ($n = 331$)	Final ($n = 165$)
Job demands	2.71 ± 1.65	2.91 ± 1.62	2.90 ± 1.62
Decision latitude	9.26 ± 1.94	9.29 ± 1.91	9.35 ± 1.92
Skill discretion	4.51 ± 0.80	4.59 ± 0.74	4.66 ± 0.68
Decision authority	4.74 ± 1.64	4.69 ± 1.66	4.68 ± 1.68
Social support	5.71 ± 1.76	5.89 ± 1.61	5.83 ± 1.65

Note. See the Method section for a description of inclusion and exclusion criteria.

ples of the Skill Discretion items are "Do your work activities vary?" and "Does your job require learning new skills?" Examples of the Decision Authority items are "Can you control your work pace?" and "Can you take a break when you feel you need one?" Social Support was assessed by seven dichotomous items referring to both coworker support and supervisor support. Examples of Social Support items are "Are your coworkers helpful in getting the job done?" and "Does your supervisor pay attention to what you are saying?" Scores on the three subscales were acquired by simply computing sum scores; "no" answers were given a score of 0, and "yes" answers were given a score of 1. Scale reliability was acceptable for Job Demands (Cronbach's $\alpha = .75$), Decision Latitude (Cronbach's $\alpha = .60$), and Social Support (Cronbach's $\alpha = .79$).

In accordance with previous studies on job strain, median values on the subscales were computed. Nurses scoring above the median on the Job Demands subscale (scores > 3) were assigned to the high-job-demands group; nurses scoring below the median on the Decision Latitude (scores < 10) or Social Support (scores < 6) subscales were assigned to the low-decision-latitude or low-social-support group, respectively.

Information on other moderators of CVD risk was obtained by a self-administered questionnaire: age, number of years involved in shift work, oral contraceptive (OC) use, alcohol consumption, smoking habits, physical activity in leisure time, physical load at work, and marital status. OC use was classified in two categories: nonusers (0) or users (1). Alcohol use was operationalized as glasses of alcohol consumed per week. Smoking habits were assessed as number of cigarettes smoked per day and classified in two categories: nonsmokers (0) and smokers (1). Physical activity in leisure time was measured with one question asking, "How many times a week during leisure time do you sweat due to physical activity?" (Gionet & Godin, 1989). Physical activity levels at work were obtained with 11 dichotomous items from the Dutch Monitor of Stress and Physical Load, referring to awkward postures and repetitive physical load (Houtman, Goudswaard, et al., 1998). Marital status was assessed from six categories, but the variable was dichotomized into married (1; which included also cohabiting with partner, family, or friends) or not married (2; which included being single, divorced, or widowed) in the statistical analyses.

Before starting the blood sampling, we asked nurses at what time they had consumed their last meal the preceding day, at what time they got up that morning, whether they had indeed been fasting since the preceding night, and the date of the first day of their last menstruation. Menstrual phase was classified in two categories: follicular phase (0; when the first day of the last menstruation was 0–14 days ago at the first blood-withdrawal day) or luteal phase (1; all others).

Statistical Analyses

All data were checked with regard to frequency distribution. Fasting insulin, TG, tPA-ag, PAI-1-ag, and body mass index were transformed to Gaussian distribution by logarithmic transformation before analysis. For readability, the back-transformed logarithmic mean and range of the transformed risk indicators are given in the descriptives. Two nurses had systolic blood pressure (SBP) values greater than 160 mmHg, which led to deviation from normality. They were excluded in all analyses on SBP.

Correlations were computed with Pearson's correlations (Spearman's correlations for categorical data). Analyses of variance were performed in a repeated-measurement general linear modeling (GLM) procedure. The dependent variables were fasting insulin, TC, HDL-C, TG, fibrinogen, tPA-ag, tPA-act, PAI-1-ag, SBP, and diastolic blood pressure (DBP). Because of the mutual correlations between the metabolic and hemostatic risk indicators, multivariate analyses were used. Independent between-subjects factors were the dichotomized scores on Job Demands, Decision Latitude, and Social Support. To test for intraweek effects, we included Day as a within-subject factor. The GLM procedure was started with a full model, which included all main effects and all higher order interactions. Subsequently, nonsignificant interactions were removed from the model

specification, and the GLM procedure was performed again. This step-down procedure ends when an exclusive significant interaction or a main effect is found (McCullagh & Nelder, 1989). To account for the large number of interaction terms, the step-down procedure was carried out against a significance level of .01.

Although dichotomization of participants in high-job-strain and no-job-strain groups has been used in previous studies, a major drawback of this method is that power to detect job-strain effects is lost by not fully exploiting the information in the full job-strain subscales. Therefore, further analysis with the continuous Job Demands, Decision Latitude, and Social Support scales was performed. Multiple stepwise regression analyses were performed for both blood-withdrawal days separately. Fasting insulin, TC, HDL-C, TG, fibrinogen, tPA-ag, tPA-act, PAI-1-ag, SBP, and DBP were used as dependent variables. Continuous scores on the subscales Job Demands, Decision Latitude, and Social Support and their products (testing linear two- and three-way interactions), OC use, age, and body mass index (BMI) were used as independent variables.

Results

Table 2 shows the mean values and standard deviations (means and ranges for back-transformed variables) of all variables for the groups high and low on job demands, decision latitude, and social support separately. The expected significant differences for job demands, decision latitude, and social support were found for the dichotomies created for these job-strain variables. Nurses with low decision latitude reported more physical activity at work and higher alcohol consumption. Nurses with low social support reported more physical activity at work and were involved in shift work for a greater number of years. No other main or interactive effects for job demands, decision latitude, or social support were found for the possible moderators of the CVD risk indicators.

Table 3 shows correlation coefficients between the Demand Control subscales; demographic, behavioral, and lifestyle variables; and metabolic and hemostatic risk indicators. BMI showed consistent associations with most risk indicators, particularly the fibrinolytic variables. Fasting insulin levels were associated with HDL-C, TG, fibrinogen, tPA-ag, tPA-act, PAI-1-ag, SBP, and DBP, in accordance with the IRS clustering.

A repeated-measurement GLM procedure was performed on the multivariate cluster of fasting insulin, TC, HDL-C, TG, fibrinogen, tPA-ag, tPA-act, PAI-1-ag, SBP, and DBP. No effects of job demands, decision latitude, social support, or their interactions were found. A highly significant day effect was found, $F(7, 149) = 10.6, p < .000$, revealing lower levels of TC, HDL-C, TG, fibrinogen, tPA-ag, and tPA-act on Day 2 (workday) compared with Day 1 (leisure day). This has been reported before (Kop, Hamulyák, Pernot, & Appels, 1998) and could reflect differences in pattern of activities on the two days, differences in noncompliance with diet across the two assessment days, habituation to the blood-drawing procedure, or unreliability of the assays. To exclude the last, test-retest reliabilities were computed. These were good (.67 for tPA-act) to excellent (.95 for TC), with a median of .86. Most importantly, this effect of weekday did not interact with job-strain parameters. Next, because of their strong influence on the levels of most of the metabolic and hemostatic risk indicators, age, BMI, and OC use were included as covariates in the full GLM model specification. Again, no effects of job demands, decision latitude, social support, or their interactions were found.

In a subsequent analysis, the nurses were assigned to more extreme job-strain groups before tests for differences on all risk

Table 2
Means and Standard Deviations of the Scores on the JCQ Subscales, Possible Moderators, and Risk Indicators for Cardiovascular Disease in 165 Female Nurses

Variable	Job demands		Decision latitude		Social support	
	Low (n = 93)	High (n = 72)	Low (n = 84)	High (n = 81)	Low (n = 74)	High (n = 91)
JCQ subscale						
Job demands	1.7 ± 1.1	4.4 ± 0.5**	3.3 ± 1.6	2.5 ± 1.5	3.4 ± 1.5	2.5 ± 1.6
Decision latitude	9.7 ± 1.9	8.9 ± 1.9	7.8 ± 1.4	10.9 ± 0.8**	8.8 ± 2.0	9.8 ± 1.7
Social support	6.2 ± 1.4	5.4 ± 1.8	5.4 ± 1.8	6.2 ± 1.4	4.4 ± 1.5	7.0 ± 0.0**
Possible moderators						
BMI (kg/m ²)	23.3 (18.2-40.6)	23.8 (18.3-39.1)	23.6 (18.2-39.1)	23.6 (18.3-40.6)	24.1 (18.7-39.1)	23.1 (18.2-40.6)
OC users (%)	39.6	50.0	45.7	43.8	52.1	38.2
Luteal phase (%)	36.4	42.9	43.2	35.6	40.0	38.2
Age (years)	34.5 ± 8.8	32.6 ± 6.9	33.7 ± 8.6	33.4 ± 7.4	33.2 ± 7.6	34.1 ± 8.5
Phys. act. at work	5.9 ± 2.9	6.9 ± 2.8	7.2 ± 2.1	5.4 ± 3.4**	7.2 ± 2.5	5.6 ± 3.1*
Active <1 day/week (%)	31.2	27.8	28.6	30.9	28.4	30.4
Not married (%)	37.6	44.4	48.8	33.3	45.9	37.0
>3 gl/w alcohol (%)	39.8	48.6	51.2	35.8*	41.9	44.6
Smokers (%)	26.9	29.2	27.4	28.4	25.7	29.3
Shift work (years)	9.6 ± 7.8	8.7 ± 6.2	9.4 ± 7.6	9.0 ± 6.7	10.3 ± 7.5	8.2 ± 6.7*
Blood pressure, metabolic, and hemostatic risk indicators						
Insulin (mU/L)	6.8 (2.8-16.5)	7.2 (4.0-24.4)	6.8 (3.1-16.1)	7.2 (2.8-24.4)	7.4 (3.1-16.5)	6.6 (2.8-24.4)
TC (mmol/L)	4.7 ± 0.9	4.8 ± 0.7	4.7 ± 0.7	4.7 ± 0.9	4.8 ± 0.8	4.6 ± 0.8
HDL-C (mmol/L)	1.46 ± 0.36	1.50 ± 0.37	1.51 ± 0.37	1.44 ± 0.35	1.48 ± 0.40	1.47 ± 0.33
TG (mmol/L)	1.00 (0.49-2.65)	1.03 (0.56-2.26)	1.02 (0.56-2.09)	1.01 (0.49-2.65)	1.07 (0.56-2.09)	0.98 (0.49-2.65)
Fibrinogen (g/L)	2.90 ± 0.51	2.84 ± 0.49	2.87 ± 0.46	2.86 ± 0.53	2.88 ± 0.49	2.87 ± 0.50
tPA-ag (ng/ml)	4.9 (1.6-16.2)	4.1 (1.5-12.4)	4.4 (1.5-12.4)	4.7 (1.7-16.2)	4.4 (1.8-12.4)	4.6 (1.5-16.2)
tPA-act (IU/ml)	0.75 ± 0.30	0.75 ± 0.29	0.73 ± 0.29	0.74 ± 0.29	0.69 ± 0.28	0.79 ± 0.30
PAI-1-ag (ng/ml)	31.5 (4.15-198.4)	24.8 (5.1-213.3)	27.1 (4.15-167.1)	29.1 (4.5-213.3)	29.4 (5.1-213.3)	27.4 (4.2-157.8)
SBP (mmHg)	122.7 ± 10.4	123.8 ± 11.1	123.56 ± 10.8	122.5 ± 10.7	124.0 ± 10.3	122.4 ± 11.0
DBP (mmHg)	73.8 ± 10.5	75.4 ± 9.6	74.3 ± 9.5	74.6 ± 10.8	75.9 ± 10.4	73.4 ± 9.8

Note. Ranges for back-transformed logarithmic means are given in parentheses. JCQ = Job Content Questionnaire; BMI = body mass index; OC = oral contraceptive; Phys. act. at work = physical activity at work; Active <1 day/week = physically active less than once a week during leisure time; >3 gl/w alcohol = drinking more than 3 glasses of alcohol a week; TC = total cholesterol; HDL-C = high-density lipoprotein cholesterol; TG = triglyceride; tPA-ag = tissue-type plasminogen activator (tPA) antigen; tPA-act = tPA activity; PAI-1-ag = plasminogen activator inhibitor-1 antigen; SBP = systolic blood pressure; DBP = diastolic blood pressure.

* $p < .05$. ** $p < .01$. Significant main effects of job demands, decision latitude, or social support.

Table 3
Correlations Between the Measured Variables in 165 Female Nurses

Variable	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
1. Job demands	—																			
2. Skill discretion	—	—																		
3. Decision authority	-.25**	.17*	—																	
4. Social support	-.26**	.27**	.23**	—																
5. BMI					—															
6. OC use	.17*			-.17*	-.19*	—														
7. Age				.25**	-.41**	—														
8. MP							—													
9. Alc. use							.16*	—												
10. Smok.		-.16*			-.21**			.35**	—											
11. Insulin				-.20*	.40**			-.23**		—										
12. TC							.18*				—									
13. HDL-C		-.18*			-.25**	.29**					-.23**	.21**	—							
14. TG						.28**		-.27*		.17*	.25**	.42**		—						
15. Fibrin.					.43**						.24**	.19*		.19*	—					
16. tPA-ag	-.17*				.40**	-.43**	.42**				.19*		-.30**							
17. tPA-act					-.49**	.32**	-.20**				-.25**		.37**		-.18*	-.43**				
18. PAI-1-ag			.16*		.49**	-.50**	.36**				.21**		-.34**		.77**	-.68**				
19. SBP					.21**						.23**								.20*	—
20. DBP						.16*					.23**			.17*				.19*	.57**	—

Note. Only significant correlations are included. Menstrual phase (MP) correlations are based only on the non-OC users ($n = 90$). BMI = body mass index; OC = oral contraceptive; Alc. = alcohol; Smok. = smoking; TC = total cholesterol; HDL-C = high-density lipoprotein cholesterol; TG = triglyceride; fibrin. = fibrinogen; tPA-ag = tissue-type plasminogen activator (tPA) antigen; tPA-act = tPA activity; PAI-1-ag = plasminogen activator inhibitor-1 antigen; SBP = systolic blood pressure; DBP = diastolic blood pressure.

* $p < .05$. ** $p < .01$.

indicators, as shown in Table 4, were performed. Nurses who simultaneously scored above the median for job demands and below the median for decision latitude were assigned to the group with high-strain jobs ($n = 41$). All others were assigned to the no-strain group ($n = 116$). Again, no job-strain-group differences were found. Including age, BMI, and OC use in the full model did not change these results.

In summary, we found no evidence for an effect of dichotomized job demands, decision latitude, social support, or their interactions, as defined by the Demand Control model, on the cardiovascular risk indicators. Only main effects of OC use, BMI, and age were found. The above dichotomies have been used in previous studies but in fact lose power to detect job-strain effects by not exploiting the information in the full scales. We therefore proceeded with regression analyses of the continuous Job Demands, Decision Latitude, and Social Support scales and their interactions. As shown in Table 5, multiple regression analyses (stepwise) revealed highly similar results for both blood-withdrawal days. None of the questionnaire subscales or their interactions contributed to the explained variance. OC use and BMI were the main predictors of all cardiovascular risk indicators studied. OC users had more favorable HDL-C, tPA-ag, tPA-act, and PAI-1-ag and more unfavorable TG and SBP levels. With increasing BMI, more unfavorable levels of all risk indicators were found. Age contributed to the explained variance of fasting insulin, HDL-C, and tPA-ag.

Discussion

The results of the present study do not support the hypothesis that job strain or job-related social support is associated with an unfavorable metabolic and hemostatic risk profile in women. Possibly, these null findings reflect a "healthy worker" effect in this population of nurses. Indeed, only a small percentage of the nurses were in the established high-risk range (Netherlands Heart Foundation, 1992; World Health Organization [WHO]/International Society of Hypertension [ISH] Mild Hypertension Liaison Committee, 1993) of TC ($1.2\% \geq 6.5$ mmol/L), HDL-C ($6.6\% \leq 0.9$ mmol/L), SBP ($7.8\% \geq 140$ mmHg), or DBP ($7.2\% \geq 90$ mmHg)

levels. The healthy profile of the nurses may in part depend on the protective function of female reproductive hormones, particularly estrogen, in premenopausal women. In the studied nurses, only 8% were postmenopausal. However, in spite of their good health, large individual variation was found in all risk indicators, and some association with job strain should have emerged even in premorbid participants, as was the case in men (Ishizaki et al., 1996; Netterstrøm et al., 1991; Vrijkotte et al., 1999). The sample size of the present study yields sufficient statistical power to detect meaningful differences between high-job-strain ($n = 41$) and no-job-strain ($n = 116$) groups. Previous cross-sectional studies of BP and fibrinogen in men, for instance, suggested effect sizes of 6.8 mmHg for SBP (Schnall, Schwartz, Landsbergis, Warren, & Pickering, 1992) and 0.24 g/L for fibrinogen (Markowe et al., 1985). This corresponded to 49% and 48% of the standard deviations of these variables, respectively. We designed our study with a more conservative effect size of 40% of the standard deviation of our risk indicators. Given our sample sizes, the power to detect group differences due to job strain or social support was 70% (based on the observed standard deviations, this corresponds to effect sizes of 4.3 mmHg for SBP and 0.20 g/L for fibrinogen).

Clearly, detection of job-strain effects also depends on the level and variation in job strain. Low job-strain levels or insufficient variation in job strain could well have attenuated its association with cardiovascular risk. Previous studies on Dutch nurses, however, have indicated that they are at risk for high work pace (Houtman & Kompier, 1995), and nurses are widely perceived to have an emotionally and physically highly demanding job (Amick et al., 1998). Empirically, the average scores and standard deviations of job demands, decision latitude, or social support in the nurses studied were similar to the ones found in a Dutch reference population of 6,485 men and women working in various jobs of the Dutch health care system, mostly nurses (Houtman, Bloemhoff, Dhondt, & Terwee, 1994; Houtman, Zuidhof, & Van Den Heuvel, 1998). It is difficult to conceive of this reference population as being restricted in range or having lower than average job strain.

We have attempted to compare our variance in job strain to the variance found in previous studies. Because different studies used

Table 4
Means and Standard Deviations of Blood Pressure, Metabolic, and Hemostatic Risk Indicators for Cardiovascular Disease for the High- and No-Job-Strain Groups

Variable	No strain			High strain ($n = 41$)
	Low strain ($n = 52$)	Passive ($n = 37$)	Active ($n = 27$)	
Insulin (mU/L)	7.0 (2.8–16.5)	6.3 (3.1–15.3)	7.5 (4.8–24.4)	7.1 (4.0–16.1)
TC (mmol/L)	4.7 \pm 1.0	4.5 \pm 0.7	4.6 \pm 0.8	4.8 \pm 0.7
HDL-C (mmol/L)	1.46 \pm 0.35	1.47 \pm 0.37	1.41 \pm 0.35	1.55 \pm 0.37
TG (mmol/L)	0.98 (0.49–2.65)	1.02 (0.58–2.08)	1.08 (0.62–2.26)	1.00 (0.56–2.09)
Fibrinogen (g/L)	2.90 \pm 0.54	2.88 \pm 0.46	2.79 \pm 0.54	2.87 \pm 0.47
tPA-ag (ng/ml)	4.9 (1.7–16.2)	4.8 (2.0–11.0)	4.3 (2.1–8.4)	4.1 (1.5–12.4)
tPA-act (IU/ml)	0.74 \pm 0.31	0.74 \pm 0.25	0.75 \pm 0.23	0.75 \pm 0.32
PAI-1-ag (ng/ml)	32.5 (4.5–198.4)	30.3 (4.2–127.8)	23.8 (5.8–213.3)	24.5 (5.1–167.1)
SBP (mmHg)	123.1 \pm 11.1	122.0 \pm 9.6	121.4 \pm 10.2	125.3 \pm 11.6
DBP (mmHg)	73.8 \pm 11.5	73.6 \pm 9.1	76.3 \pm 9.4	74.8 \pm 9.8

Note. Ranges for back-transformed logarithmic means are given in parentheses. TC = total cholesterol; HDL-C = high-density lipoprotein cholesterol; TG = triglyceride; tPA-ag = tissue-type plasminogen activator (tPA) antigen; tPA-act = tPA activity; PAI-1-ag = plasminogen activator inhibitor-1 antigen; SBP = systolic blood pressure; DBP = diastolic blood pressure.

Table 5
Multiple Regression Analyses (Stepwise) of Cardiovascular Risk Indicators on Days 1 and 2

Risk indicator	Predictor 1			Predictor 2			Predictor 3			Total R ²
	Predictor	β coef.	p value	Predictor	β coef.	p value	Predictor	β coef.	p value	
Day 1										
Insulin	BMI	.497	.000	Age	−.265	.000	Age	.171	.040	.249
HDL-C	OC	.291	.001	BMI	−.226	.004				.133
TG	OC	.327	.000	BMI	.234	.003				.130
Fibrinogen	BMI	.449	.000	OC	.203	.009	Age	.179	.017	.200
tPA-ag	OC	−.286	.000	BMI	.299	.000				.304
tPA-act	BMI	−.401	.000	OC	.174	.019				.219
PAI-1-ag	OC	−.391	.000	BMI	.387	.000				.365
Day 2										
Insulin	BMI	.413	.000	Age	−.268	.000	Age	.221	.003	.197
HDL-C	OC	.234	.003	BMI	−.184	.019				.107
TG	OC	.257	.001							.066
Fibrinogen	BMI	.452	.000				Age	.221	.003	.204
tPA-ag	OC	−.282	.000	BMI	.279	.000				.318
tPA-act	BMI	−.427	.000	OC	.235	.001				.278
PAI-1-ag	OC	−.405	.000	BMI	.400	.000				.390
SBP	BMI	.219	.006							.048
DBP	OC	.182	.024							.051

Note. Predictors were job demands, skill discretion, decision authority, social support, and their two-way and three-way interactions; age; body mass index (BMI); and oral contraceptive (OC) use. Coef. = coefficient; HDL-C = high-density lipoprotein cholesterol; TG = triglyceride; tPA-ag = tissue-type plasminogen activator (tPA) antigen; tPA-act = tPA activity; PAI-1-ag = plasminogen activator inhibitor-1 antigen; SBP = systolic blood pressure; DBP = diastolic blood pressure.

different scales, we computed coefficients of variation ($CV = \text{standard deviation/mean score}$), which were 55% for job demands, 20% for decision latitude, and 29% for social support. Of the studies with positive results in women, only one (Wamala, Wolk, Schenk-Gustafsson, & Orth-Gomér, 1997) reported means and standard deviations, but only for decision latitude ($CV_{\text{decision latitude}} = 39\%$). In conclusion, in spite of the homogeneous occupational setting, lack of variation on the Demand Control scales or low scores are not a compelling reason for not finding an association between job strain and CVD risk.

Can our results be reconciled with the evidence showing job strain to predict CVD and mortality? It must first be noted that many possible risk factors mediating job-strain effects were not tested in this study; for example, no assessment was made of cardiovascular hyperreactivity to work-related stresses. Such reactivity has been associated with increased risk for CVD in premenopausal female cynomolgus monkeys (Williams, Shively, & Clarkson, 1994) and in human females (Kral et al., 1997). Although we cannot rule out the possibility that job-strain effects are mediated by these and other unmeasured risk factors, our data are also compatible with alternative, more parsimonious explanations: To date, the predictive value of the Demand Control model for CVD is largely validated in heterogeneous occupational populations (Theorell & Karasek, 1996). In such populations, significant associations are found between job strain and level of education (Theorell, Ahlberg-Hultén, Jodka, Sigala, & De La Torre, 1993) and SES (Wamala, Wolk, & Orth-Gomér, 1997). These factors have repeatedly been shown to increase CVD risk (Marmot & Theorell, 1988; Wamala, Wolk, & Orth-Gomér, 1997). Consequently, it has been suggested that job strain might not be predic-

tive for CVD in a homogeneous occupational population because the ranges of SES and level of education in such populations are restricted (Carayon, 1993; Payne & Fletcher, 1983). The ranges of SES and educational background were indeed restricted in our nurses, and this may have eliminated job-strain effects on the risk indicators entirely.

Another potential reason for the lack of relationships between job strain and CVD risk indicators may be the age of the cohort studied: 22–55 years. Although there was no interaction between age and job strain, it is possible that job-strain effects would have emerged in a cohort of older nurses. Previous studies with women that did report physiological effects of job strain always measured older women (Davis et al., 1995; Peter et al., 1998; Wamala, Wolk, Schenk-Gustafsson, & Orth-Gomér, 1997), whereas studies of younger cohorts always reported null findings (Folsom et al., 1993; Greenlund et al., 1995; Weidner et al., 1997). Although some studies in older women also reported null findings (Gyntelberg et al., 1998; Netterstrøm et al., 1991; Tsutsumi et al., 1999), this pattern of results suggests that an association between job strain and the CVD risk indicators can be found only in middle-aged and older women. Further research is necessary to confirm this hypothesis, since the positive studies (a) left out information about the hormonal status of the studied women (Peter et al., 1998) or when hormonal status was precisely assessed, (b) included only non-OC-using women (Davis et al., 1995), or (c) assessed no data on OC use (Wamala, Wolk, Schenk-Gustafsson, & Orth-Gomér, 1997).

Finally, the "toxic" ingredient of chronic stress may not be completely identified by job strain alone. Johnson et al. (1996) suggested that low control over the work process is the true toxic

ingredient of the work environment. This suggestion received further support from Bosma et al. (1997), who showed that in women, only low decision latitude, and not job demands or social support, was predictive of coronary heart disease (CHD). However, in the present study, decision latitude did not affect CVD risk indicators, suggesting that refinement of the job-strain concept in women is needed. Two candidates for such a refinement are the "double" workload and individual differences in patterns of appraisal and coping with work-related stress. Working women still retain primary responsibility for most of the domestic work and child care (Light, 1997; Lundberg, 1998), and interactions with job-related obligations may be expected. Patterns of appraisal can be measured by the Effort Reward Imbalance model (Siegrist et al., 1990), which uses two summary measures of work stress: (a) imbalance, the ratio between extrinsic effort (demands on the job) and rewards (money, esteem, and status control); and (b) overcommitment, a psychological coping style associated with the inability to withdraw from work obligations (Siegrist & Peter, 1994). In the Whitehall II data, Bosma et al. (Bosma, Peter, Siegrist, & Marmot, 1998) found that effort-reward imbalance and low job control were independently related to CHD in men and women.

In contrast to job strain, significant effects of age, BMI, and OC use were found on most of the risk indicators. Surprisingly, BMI and OC use, not age, were the strongest correlates of metabolic and fibrinolytic risk. In fact, the age-related effects on fibrinolysis may not be a primary effect of aging but may be secondary to decreases in OC use or increases in body weight (DeSouza, Jones, & Seals, 1998). The previous studies on fibrinolysis and OC use are conflicting, but a reduction of plasma PAI-1-ag appears to be the most robust finding in OC users (De Paz et al., 1995; Quehenberger, Kapiotis, & Partan, 1993; Siegbahn & Ruusuvaara, 1988). The inverse relationship between circulating PAI and OC use found in the present study is in accordance with this and is probably due to the inhibitory effects of OC use on PAI production or release from the endothelial cells (Kluft & Lansink, 1997; Siegbahn & Ruusuvaara, 1988). The association of BMI with the IRS variables is in agreement with previous findings (Brindley & Rolland, 1989; Reaven, 1988, 1996) and strengthens the idea that adipocytes, besides being fat-storage cells, may synthesize and secrete a variety of molecules—for example, lipoproteins, coagulation variables, and cytokines—and contribute to the thrombotic and cardiovascular risk associated with fatness (Loskutoff & Samad, 1998). In contrast to the suggestion that stress influences dietary pattern (Wing, Matthews, Kuller, Meilahn, & Plantiga, 1991) and body-fat storage (Björntorp, 1997), no evidence was found in the present study of an association of job strain with BMI.

Chronic job strain can be emotionally demanding in a way that influences psychological health, quality of life, productivity, or sickness absence (Houtman et al., 1999), which makes interventions important from an organizational point of view. However, if changes in cardiovascular risk are the primary target, our results suggest that the toxic ingredient of chronic stress in a homogeneous sample of working women still needs to be identified, at least with regard to the risk indicators measured. Pending refinement of the job-strain concept, interventions aimed at these risk indicators should focus on reducing body weight, for example, by

means of changing diet habits (Ginsberg et al., 1998) and stimulating a physically active lifestyle (DeSouza et al., 1998). As a final note, these results apply to young female nurses and need not generalize to older nurses or women employed in other homogeneous job settings.

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